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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/630,930	07/31/2003	Satoshi Arakawa	Q76759	9500

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EXAMINER

PERREIRA, MELISSA JEAN

ART UNIT PAPER NUMBER

1618

DATE MAILED: 06/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/630,930	ARAKAWA, SATOSHI	
	<b>Examiner</b>	<b>Art Unit</b>	
	Melissa Perreira	1618	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 31 July 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 7/31/03 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)               | Paper No(s)/Mail Date. _____  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>7/31/03</u> 10 - 23 - 03  | 6) <input type="checkbox"/> Other: _____                                    |

## **DETAILED ACTION**

### ***Specification***

1. The disclosure is objected to because of the following informalities: The specification recites Figure 1, Figure 2 and Figure 3 while the drawings are labeled FIG.1, FIG.2 and FIG.3. Please correct the specification throughout to match the labeled figures.

### ***Claim Rejections - 35 USC § 103***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakajima et al. (US 4,710,875) in view of Aikawa et al. (US 2003/0180220).

3. Nakajima et al. (US 4,710,875) teaches of a subtraction process method classified as a temporal (time difference) subtraction processing method. An image of a specific structure is extracted by subtracting the digital image signal of an X-ray image obtained without injection of a contrast media from the digital image signal of an X-ray image in which the image of the specific structure is enhanced by the injection of a contrast media (column 2, lines 25-47). In the aforesaid radiation image system a stimuable phosphor sheet is used and it is possible to conduct various digital processing since a final radiation image can be reproduced on various output devices and processing of the signal can be done in various ways (column 3, lines 32-45).

Nakajima et al. (US 4710875) does not teach of a liposome contrast agent containing a hydrophobic iodine derivative, a phosphatidyl choline and a phosphoric dialkyl ester.

4. Aikawa et al. (US 2003/0180220) teaches of an X-ray contrast agent and its administration. The disclosed liposome contains a hydrophobic iodine compound in which cholesterol is bound to a 1,3,5-triiodobenzene, a phosphatidyl choline and phosphatidyl serine and a phosphoric acid dialkyl ester such as dicetyl phosphate (p 2, column 1, paragraphs 2-3; p 3, column 2, paragraph 2; p 5, column 1, paragraph 3). The liposome can be used in, but not limited to the detection of vascular disease, such as arteriosclerosis by visualizing vascular flows and detecting a lesion at which the flows are obstructed. This provides for a non-invasive method of selectively accumulating the contrast agent in the desired cells and provides a means for imaging a biological environment (p 1, column 2, paragraph 6). At the time of the invention it would have been obvious to one ordinarily skilled in the art to use the selective and non-invasive contrast agent; liposome containing a hydrophobic 1,3,5-triiodo benzene derivative taught by Aikawa et al. (US 2003/0180220) with the subtraction process method taught by Nakajima et al. (US 4710875) to develop an improved subtraction process method for the detection of arteriosclerosis.

5. Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakajima et al. (US 4,710,875) in view of the combined teachings of Mackaness et al. (US 4,192,859) and Xiao et al. (*Pharm. Res.* **1999**, 16, 420-426).

6. Nakajima et al. (US 4,710,875) teaches of a subtraction process method classified as a temporal (time difference) subtraction processing method. An image of a

specific structure is extracted by subtracting the digital image signal of an X-ray image obtained without injection of a contrast media from the digital image signal of an X-ray image in which the image of the specific structure is enhanced by the injection of a contrast media (column 2, lines 25-47). In the aforesaid radiation image system a stimutable phosphor sheet is used and it is possible to conduct various digital processing since a final radiation image can be reproduced on various output devices and processing of the signal can be done in various ways (column 3, lines 32-45).

Nakajima et al. (US 4710875) does not teach of a liposome contrast agent containing a hydrophobic iodine derivative, a phosphatidyl choline and a phosphoric dialkyl ester.

7. Mackaness et al. (US 4,192,859) teaches of an X-ray contrast media, such as a hydrophobic iodine derivative and a liposome as a carrier thereof (abstract). Liposomes employed in the present invention generally comprise lipid material of the phospholipid types, such as cholesterol and with or without a charged component of dicetyl phosphate (column 3, paragraph 4-5). A preparation of a liposomal mixture consists of phosphatidyl choline, cholesterol, 2,4,6-triiodobenzene derivative as well as others listed above (Example 1, column 4). Mackaness et al. (US 4,192,859) does not teach of a liposome contrast agent containing a hydrophobic 1,3,5-triiodobenzene derivative.

8. Xiao et al. (*Pharm. Res.* **1999**, *16*, 420-426) teaches of cholesteryl iopanoate (1,3,5-triiodobenzene derivative) and its incorporation into AcLDL for the early and non-invasive detection of atherosclerosis. The microemulsion consists of a mixture of cholesteryl iopanoate and L- $\alpha$ -phosphatidylcholine dipalmitoyl for the selective uptake and retention of cholesteryl iopanoate at the site of atherosclerotic lesion.

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9. At the time of the invention it would have been obvious to one ordinarily skilled in the art to use the combined teaching of Mackaness et al. (US 4,192,859) of a selective and non-invasive hydrophobic iodine derivative contrast agent and substitute a cholesteryl iopanoate (1,3,5-triiodobenzene derivative) taught by Xiao et al. (*Pharm. Res.* **1999**, *16*, 420-426) where the selective uptake and retention of the contrast media at the site of atherosclerotic lesion has been successfully achieved. The subtraction process taught by Nakajima et al. (US 4,710,875) can be used with the improved cholesteryl iopanoate contrast agent to develop an improved subtraction process method for the detection of arteriosclerosis.

### ***Conclusion***

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melissa Perreira whose telephone number is 571-272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MP  
May 24, 2006

  
MICHAEL G. HARTLEY  
SUPERVISORY PATENT EXAMINER